

FAMILIAL CARDIOMEGALY

BY

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When valvular, hypertensive, and congenital heart disease have been excluded as causes of cardiac enlargement, some rarer condition should be sought, but only after excluding bradycardia, pericardial disease, sternal depression, or an elevated diaphragm, which by themselves without real enlargement produce an exaggerated cardiac silhouette on cardioscopy. Such being eliminated, there remains a group where the cause of cardiac enlargement is obscure, and it is the purpose of this paper to describe cases with common subjective and objective symptoms, and to propose a syndrome that serves to explain a hitherto ambiguous form of cardiac enlargement and facilitates clinical diagnosis of the condition.

NOTES OF THREE CASES IN ONE FAMILY

Case 1. Male, aged 18 years. He was referred by a service medical board which sought an explanation for the displacement of his apex beat. He admitted to no symptoms at the time and he appeared to be a well-developed healthy youth. The pulse was irregular from extrasystoles with brief periods of paroxysmal tachycardia. The blood pressure was 120/80. The apex beat was forcible and was displaced as far as the left anterior axillary line. The heart sounds were clear and there were no murmurs. A triple rhythm was present from the addition of the third heart sound. There was no enlargement of the liver or spleen, and further examination found no abnormal signs elsewhere including the central nervous system. The Wassermann reaction was negative. The blood sugar and cholesterol were both normal, and so was the sugar tolerance test; there was no ketosis. The cardiogram (Fig. 1) showed extrasystoles and exceptionally wide QRS complexes with inverted T waves. On cardioscopy (Fig. 3) there was great enlargement of the heart, and particularly of the left ventricle; the border of which was remarkably quiet compared with the mobile right auricle.

While under observation for two months, the extrasystoles became more frequent and when attacks of paroxysmal tachycardia increased in number and severity, the patient was handicapped in his work at times by giddiness. At last, when tachycardia (Fig. 2) persisted for two days, pulmonary oedema (Fig. 4) developed and he died on the third day.

Summary of Necropsy (P.M. 121/1947). By Professor Dorothy Russell of the Bernhard Baron Institute of Pathology.

Acute pulmonary oedema. Heart failure. Familial Cardiomegaly. Clear yellow pericardial effusion (4 oz.). Slight whitish opacity of most of visceral pericardium over both ventricles. Milk-spot (2.5 by 1.2 cm.) on anterior surface of right ventricle. Foramen ovale patent (about 1 cm. diameter), the orifice being valvular. Great thickening (up to 4 cm.) of myocardium of left ventricle, without appreciable dilatation, composed of pale brown moderately firm tissue blotched with numerous ill-defined pale areas of fibrosis (Fig. 5). Similar proportionate thickening of other chambers of heart (Fig. 6); but least marked of left auricle (5 cm. diameter; 0.4 cm. thick). All valves normal apart from congenital fenestration of two pulmonary cusps. Coronary arteries normal and enlarged in proportion to ventricles; no atheroma. Aorta of normal circumference (6 cm. at ring, and 0.2 to 0.25 cm. thick). Very slight atheroma. Early mucinous degeneration of media of aorta found microscopically.

Clear yellow pleural effusions (right, 12 oz.; left, 5 oz.). Almost solid oedema of right lung, showing microscopically variable numbers of red corpuscles and phagocytes in alveolar spaces; purulent bronchitis and early broncho-pneumonia present in a few places. Left lung similar but showing, microscopically, a layer of fibrin coating respiratory bronchioles and some alveoli. Enlargement of gland at tracheal bifurcation, and another above right bronchus, by miliary and larger caseous

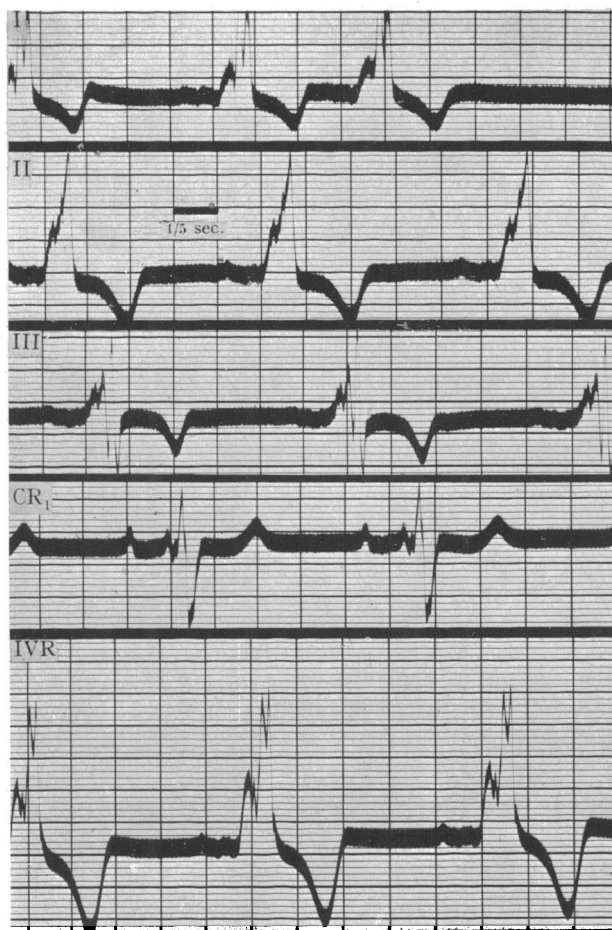


FIG. 1.—Electrocardiogram from Case 1. Sinus rhythm with extrasystoles; exceptionally wide QRS complexes with four R waves showing in IVR, and deep inversion of the T waves in many leads.

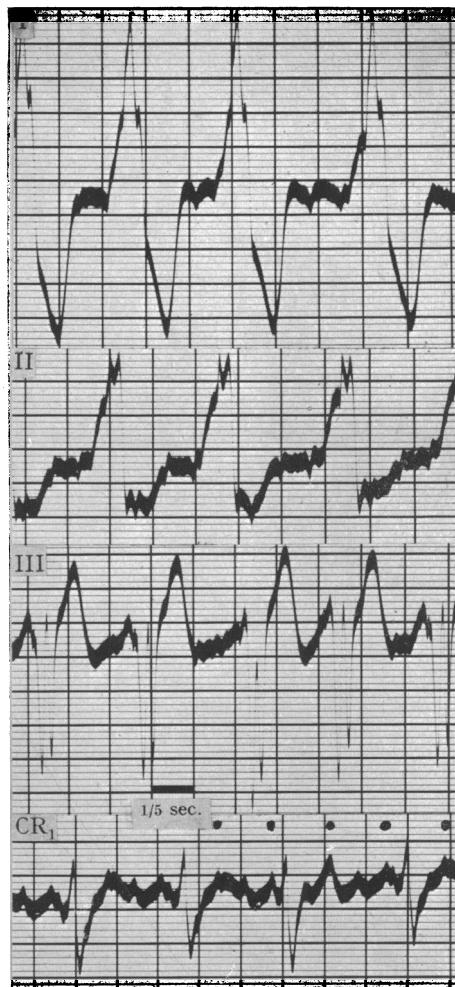


FIG. 2.—Electrocardiogram from Case 1. Paroxysmal tachycardia with a high auricular rate and A-V dissociation.

tubercles, with considerable focal fibrosis. No tuberculosis found in lungs. Central congestion of liver. Chronic congestion and oedema of spleen, showing microscopically two miliary tubercles in pulp. One old infarct in spleen and one in right kidney. Congestion and severe post-mortem degeneration of kidneys. Persistent glandular thymus. No abnormality, macroscopic or microscopic, in endocrine glands. (Only one parathyroid identified.) Post-mortem digestion of stomach. No macroscopic or microscopic abnormality found in brain or spinal cord. Middle ears normal. Cyanosis of extremities. No sub-

cutaneous oedema. A well developed and well nourished young man.

Weights. Body, 62.5 kg. (height, 1.7 m.); heart, 1134 g.; liver, 1921 g.; kidneys, 333 g.; spleen, 333 g.; brain, 1495 g.; suprarenals, 13 g.; thyroid, 56 g.; thymus, 20 g.; testes, 21 g.; pituitary, 0.6 g.

Microscopic examination. Portions of the left ventricle and right auricle were fixed in Bouin's fixative. The rest of the heart was fixed in formaldehyde, blocks being taken on the following day from both ventricles, interventricular septum, and sino-auricular node. In addition to hæmatoxylin and

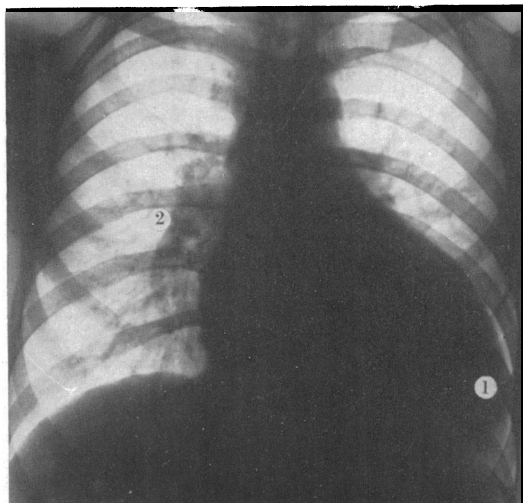


FIG. 3.—Teleradiogram from Case 1. Great enlargement of the heart and especially of the left ventricle (1); much pulmonary congestion (2).

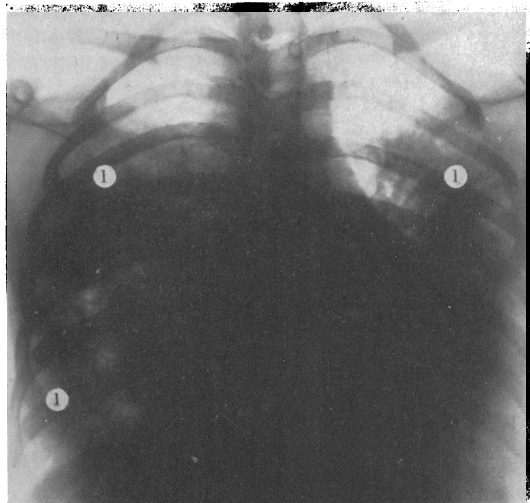


FIG. 4.—Teleradiogram from Case 1. Pulmonary oedema (1) is added to the great cardiac enlargement seen in Fig. 3.

eosin, iron hæmatoxylin and van Gieson and phosphotungstic-acid hæmatoxylin, sections from all blocks were stained by Best's carmine for glycogen. Frozen sections of a piece of left ventricle were stained with Sudan III for fat.

Heart. In all parts examined there is dense patchy fibrosis of the myocardium, especially beneath the endocardium and pericardium, and gross hypertrophy of the muscle fibres (Fig. 7). The hypertrophy often appears greatest where there is most fibrosis. In ordinary stains the fibres are occasionally greatly vacuolated, but vacuolation in general is rather inconspicuous, except in phosphotungstic-acid hæmatoxylin preparations, where high magnifications frequently reveal clusters of small vacuoles in the centres of fibres, or groups of reddish-brown granules in a similar situation. In such fibres the longitudinal fibrils are restricted to the periphery of the muscle cell and cross-striation is lost. Cross-striation is preserved in many fibres devoid of vacuoles and granules. There is no fatty degeneration. The Bouin-fixed sections show conspicuous deposits of glycogen in many scattered fibres in both left ventricle and right auricle. There are no circumscribed areas in which all or most fibres are so affected; the change is diffuse. A good deal of finely granular material stained by Best's carmine is present in the intermuscular connective tissue and in the walls of capillaries. In the formalin-fixed tissue, however, there is little evidence of glycogen. The fibrous tissue in the myocardium contains few

spindle cells and occasional small lymphocytes which are mostly perivascular. Occasional larger clumps of small round cells appear to be due to submiliary granulomatous tubercles, one being identified with certainty in the interventricular septum, and one in the pericardium of the left ventricle. The pericardium elsewhere is little affected; there are a few small lymphocytes about the vessels, which are engorged. No changes were found in the special muscle fibres of the conducting system.

Liver. In a block fixed in Bouin's fluid there is great congestion and atrophy of the centres of the lobules; in places adjacent atrophied areas are confluent. There is no fibrosis. A good deal of glycogen is present as fine cytoplasmic granules in the better preserved cells of the periportal parenchyma.

Muscle. Portions of the tongue and vastus externus muscle were fixed in Bouin's fluid. In the tongue glycogen is restricted to the squamous epithelium and some cells of the mucous glands. In the vastus externus large quantities of glycogen are present, some being in the muscle fibres but most has escaped into the interstitial tissue. Patchy vacuolation of the fibres is demonstrated by other stains, but the degree of vacuolation appears trivial in comparison with the amount of glycogen. A special search for glycogen was made in Bouin-fixed material from the kidney, spleen, and central nervous system with negative results.

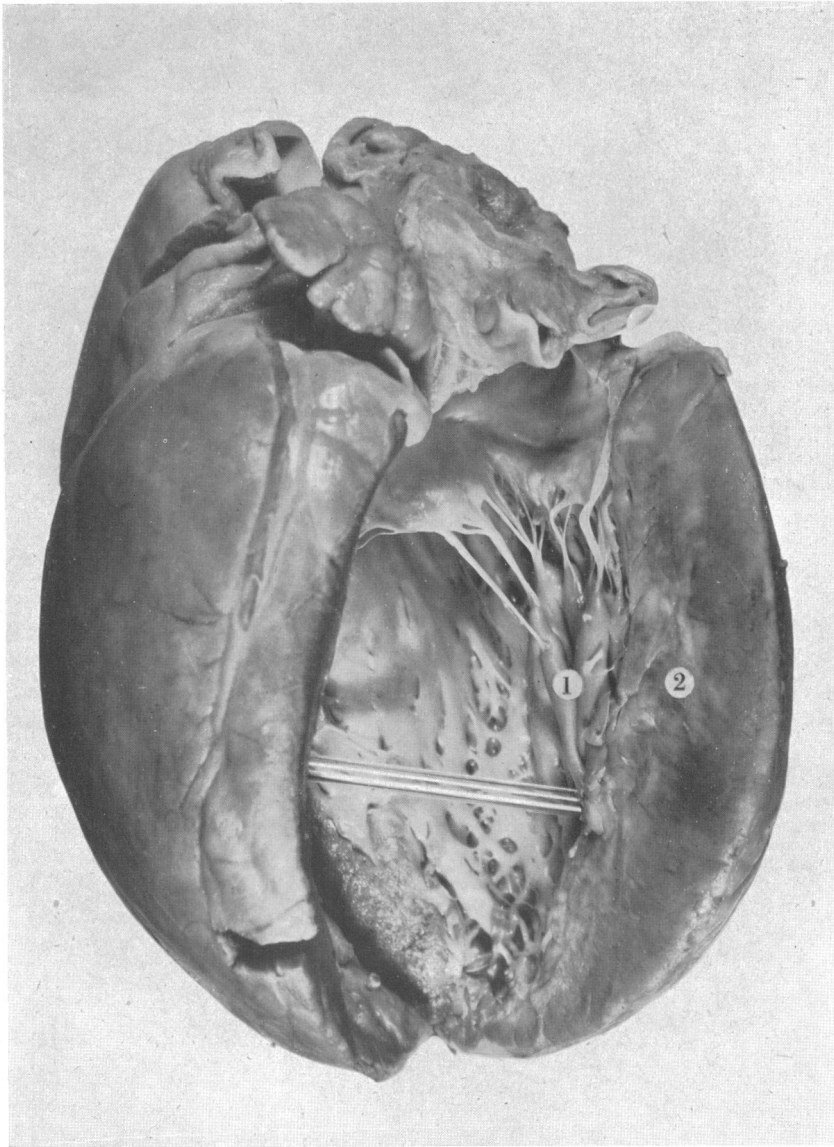


FIG. 5.—Photogram of the heart in Case 1. There is very great general hypertrophy and especially of the left ventricle (1) which shows grey patches of fibrosis (2).

Case 2. Male, aged 20 years. His appearance was healthy and he complained of no symptoms when he was referred by a service medical board because of great outward displacement of the apex beat. Later, he admitted that during the past six months he had been compelled through giddiness to halt the omnibus he drove, but had never lost consciousness. The pulse was normal in rate and irregular from auricular fibrillation. The blood

pressure was 125/80. The apex beat was near the left anterior axillary line and was forcible. The heart sounds were clear and there were no murmurs. Triple heart rhythm was present from addition of the third heart sound. There was no enlargement of the liver, nor of the spleen, and on examination the other systems, including the nervous system, were normal. The blood sugar and the blood cholesterol were both normal. The electrocardiogram showed

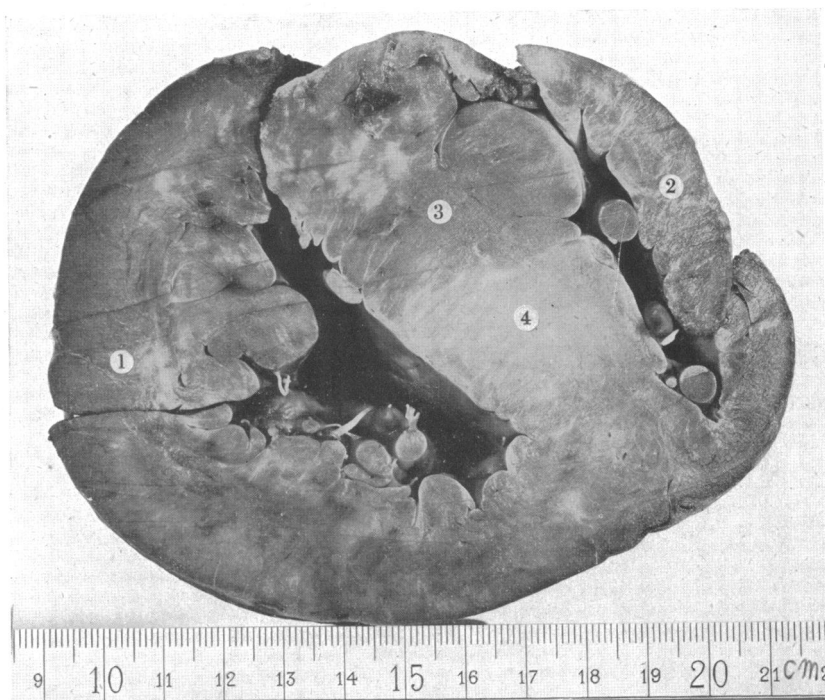


FIG. 6.—Cross-cut of the heart in Case 1 to show great hypertrophy of the left ventricle (1), right ventricle (2), and the septum (3), which shows extensive fibrosis (4).

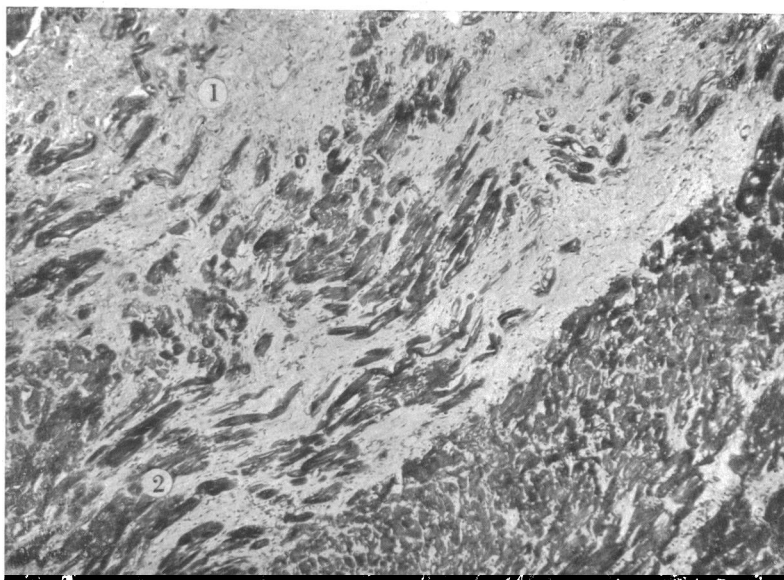


FIG. 7.—Microscopical section of the myocardium from Case 1, showing great fibrosis (1) and hypertrophy of surviving muscle fibres (2).



FIG. 8.—Electrocardiogram from Case 2. Auricular fibrillation; wide QRS complexes with deep inversion of the T waves in all leads.

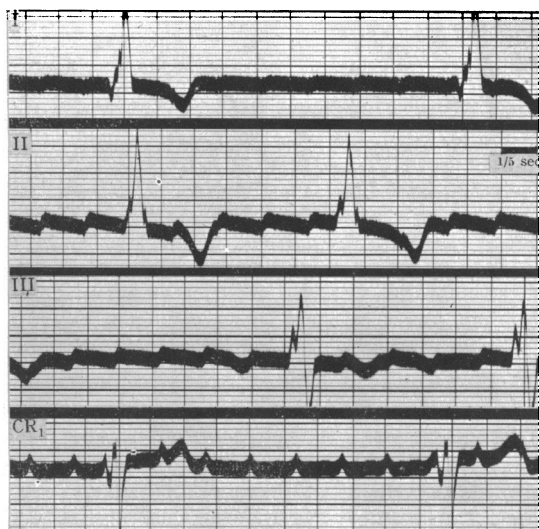


FIG. 9.—Electrocardiogram from Case 2. Auricular flutter with slow ventricular rate. Varying A-V dissociation.

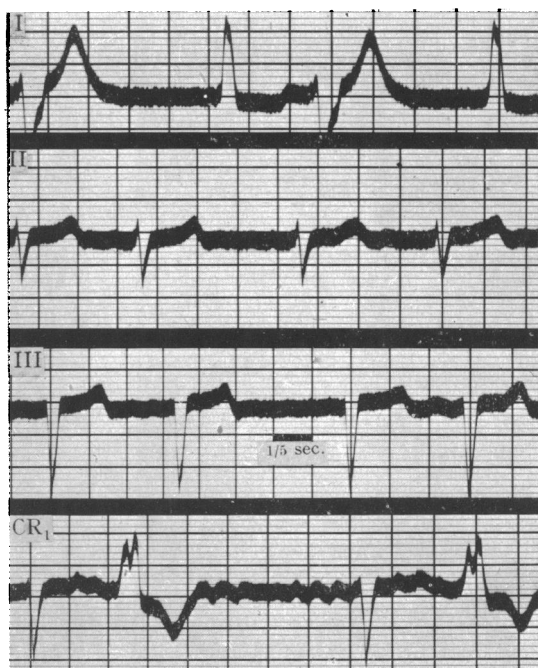


FIG. 10.—Electrocardiogram from Case 3. Auricular fibrillation and extrasystoles; the T wave is inverted in lead I, and the R wave is small in CR1.

auricular fibrillation, exceptionally wide QRS complexes, and deeply inverted T waves (Fig. 8). Another time (Fig. 9) he showed auricular tachycardia with infrequent ventricular rate. On cardioscopy (Fig. 11) there was great enlargement of the heart, and particularly of the left ventricle, the left border of which was remarkably quiet compared with the pulsatile right auricle at the opposite cardiac border.

Case 3. Female, aged 43 years. For 12 years she had suffered from infrequent but severe syncopal attacks. Her pulse was about 70 a minute and was irregular from auricular fibrillation. The blood pressure was 130/90. The apex beat was displaced outwards and was forcible. The heart sounds were clear and there were no murmurs. There was conspicuous splitting of the second heart sound and this was confirmed by the phonocardiogram. There was no enlargement of the liver nor spleen, and examination of other systems showed no abnormal signs. There were extrasystoles and auricular fibrillation with inversion of the T I (Fig. 10). On cardioscopy (Fig. 12) there was moderate enlargement of the heart, and especially of the left ventricle.

These three patients illustrate the familial and hereditary nature of the illness; Cases 1 and 2 were brothers and were the sons of Case 3, whose husband

and a third son, aged 17 years, were healthy; an infant son had died at the age of 18 months from "heart trouble"; her parents died at the ages of 34 and 35, but the manner of their deaths could not be ascertained; a brother and sister as well as their offspring were healthy; one sister died suddenly in a tramcar at the age of 26 although she was thought to be healthy up to that time; another sister died unexpectedly at the age of 30; a brother while on his way to work one morning dropped dead on the pavement at the age of 21; details of necropsy in these cases cannot be traced, but the manner of their deaths makes it likely that at least six members in two generations of the same family suffered from the condition that is described here (Fig. 13). A family history of the same illness was also obtained from a patient reported at the Massachusetts General Hospital (1942) and also in one described by Addarii and Mahaim (1946).

In addition to the three cases already described there were six others whose symptomatology and clinical signs were so similar as to make me believe that they suffered from the same condition. In one where a necropsy was carried out, fibrosis of the myocardium was found to be the underlying lesion as in Case 1, but no family history of the condition could be obtained from any of the six cases, although in none had it been possible to examine other members of the family.

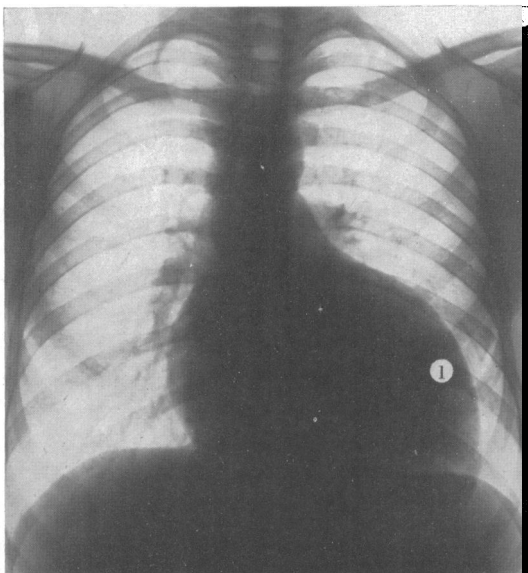


FIG. 11.—Teleradiogram from Case 2 showing great general enlargement of the heart and especially of the left ventricle (1).

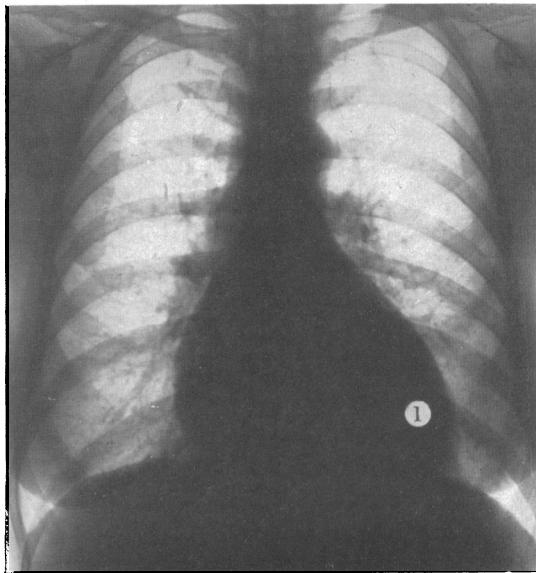


FIG. 12.—Teleradiogram from Case 3 showing moderate general enlargement of the heart, and especially of the left ventricle (1).

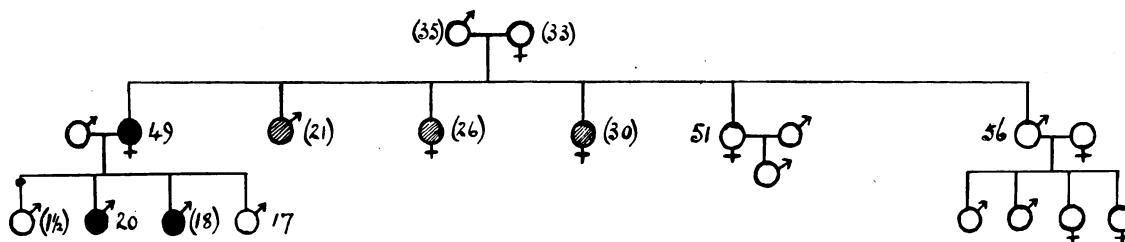


FIG. 13.—Scheme identifying patients affected with Familial Cardiomegaly in one family. The black symbols represent members suffering from familial cardiomegaly; the shaded symbols indicate members probably affected by the same illness; the unshaded symbols are unaffected members. The numerals are the ages in years, and when bracketed they indicate the age at death.

OTHER CASE NOTES

Case 4. Male, aged 35 years. Two years before he was rejected for military service by a medical board which advised him not to do any heavy work. He remained well until a month before when he fainted in a chair and afterwards discovered a lump on the back of his head which he supposed had resulted from his head falling backward on to the chair. Thereafter he experienced spells of giddiness which made him uncertain of himself when walking, but when they passed he would feel quite well. Only once did he lose consciousness. No other members of the family were similarly affected.

His appearance was healthy. The pulse was slow (52 a minute), and was irregular from extrasystoles, which disappeared for a short time after exercise.

The blood pressure was 115/70. The apex beat reached the anterior axillary line and was forcible in character with a double impulse. There was no thrill. A triple heart rhythm was present from the addition of the third heart sound and this was confirmed by the phonocardiograph. There were no murmurs. Further routine clinical examination showed no abnormal signs in other systems. The electrocardiogram (Fig. 14) showed bradycardia, bundle branch block, and extrasystoles. On cardioscopy (Fig. 16) there was great generalized enlargement of the heart. The Wassermann reaction was negative. He continued with his work, but complained of giddiness on occasions. Three years later there was another syncopal attack, but he recovered only to fall dead as he was walking home from work. There was no necropsy.

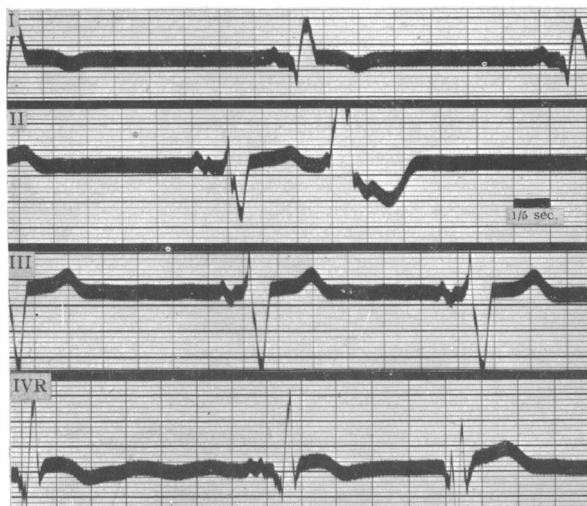


FIG. 14.—Electrocardiogram from Case 4. Sinus bradycardia with extrasystoles; wide QRS complexes; prominent Q, R-T deviation, and inversion of the T wave in lead I; Q wave, and R-T deviation in IVR.

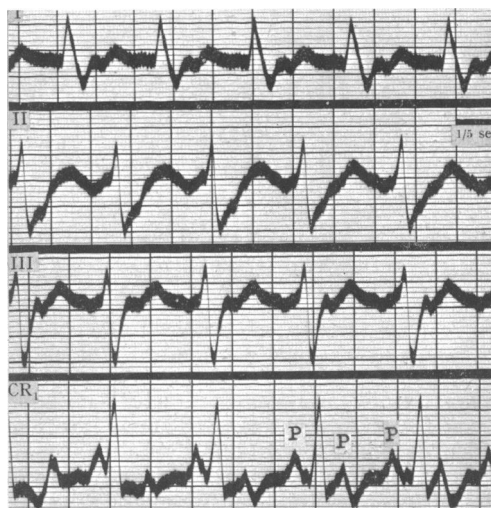


FIG. 15.—Electrocardiogram from Case 5 during an attack of paroxysmal tachycardia with 2 to 1 A-V dissociation which is best seen in CR1.

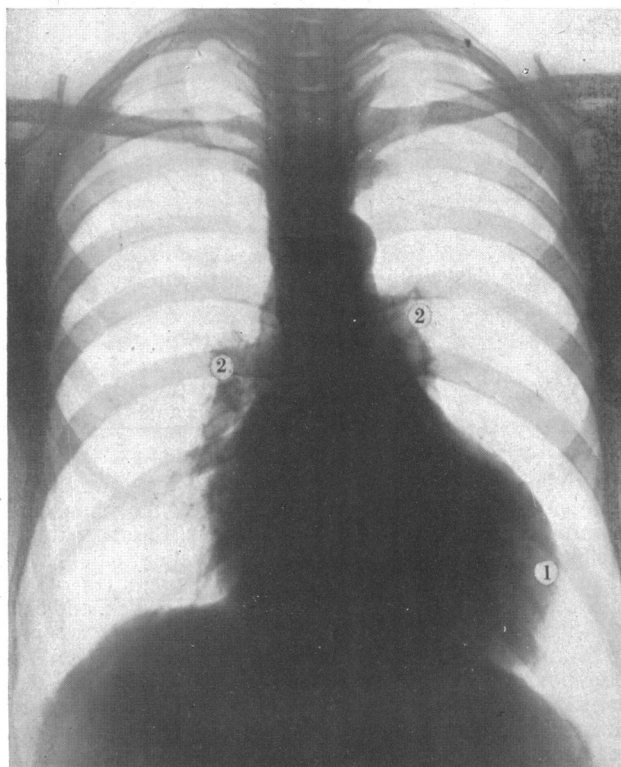


FIG. 16.—Teleradiogram from Case 4. Great enlargement of the heart and especially of the left ventricle (1); pulmonary congestion (2).

Case 5. woman, aged 63 years. Three years before, she complained of dizziness and at times lost consciousness. Later, palpitation became troublesome and she said that the heart occasionally beat very rapidly. The pulse was 56 and irregular from extrasystoles, and she was sometimes found with paroxysmal tachycardia. There was no hypertension. The apex beat was displaced outwards as far as the anterior axillary line and it was diffuse and forcible. There was an obvious triple heart rhythm from addition of the third heart sound. A systolic murmur in the mitral area occupied mid-systole and there were no diastolic murmurs. Although the thyroid was enlarged, there were no signs of thyroid toxæmia. There were no abnormal signs in any other system. At one time sinus bradycardia with ventricular complexes of bundle branch block, and at other times paroxysmal tachycardia with 2 to 1 (Fig. 15) or a higher grade A-V dissociation, were seen. On cardioscopy (Fig. 17) there was great enlargement of the heart, particularly of the right side. She is still alive.

Case 6. Woman, aged 62 years. She was ad-

mitted to hospital for attacks of palpitation 15 years ago; although the arrhythmia did not recur in hospital, radiological examination showed enlargement of the heart. Throughout the years she continued to experience these attacks and in two of them she lost consciousness. Two years ago an electrocardiogram showed sinus bradycardia and bundle branch block. Twelve months ago a cardiogram during the attack showed auricular fibrillation and she again reverted to normal rhythm. There were more episodes of paroxysmal auricular fibrillation, and unconsciousness once from cerebral embolism. She gradually recovered from the paralysis and for three months she had not experienced any palpitation while the heart rhythm continued as auricular fibrillation with infrequent ventricular rate. The cardiogram showed right bundle branch block in addition to fibrillation. The blood pressure was normal. The apex beat was out a little way and there was moderate cardiac enlargement. No triple heart rhythm was present at the single clinical examination. There was no enlargement of the liver or spleen and the urine was clear. Since the auricular fibrillation became established the syncopal attacks had become less frequent.

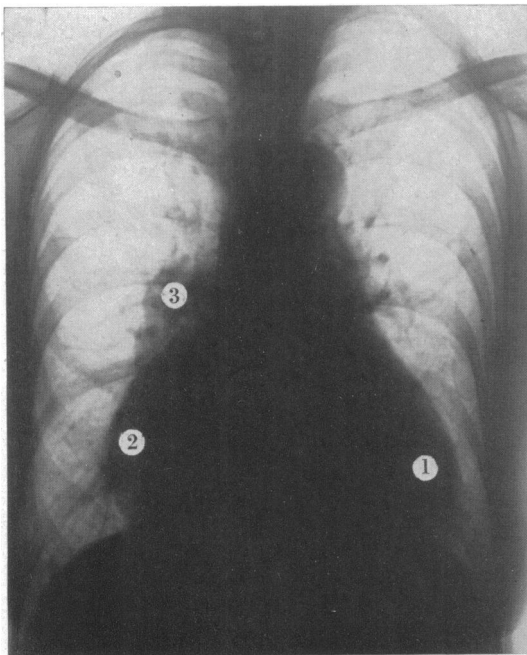


FIG. 17.—Teleradiogram from Case 5. There is enlargement of the left ventricle (1) and especially of the right auricle (2). Pulmonary congestion (3).

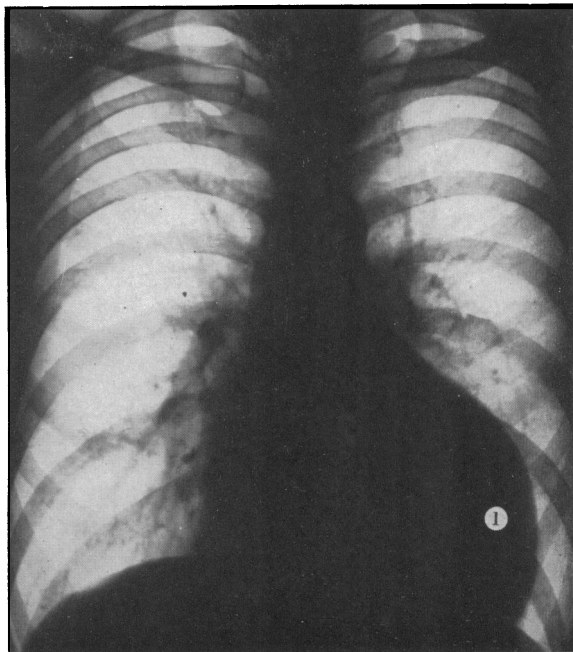


FIG. 18.—Teleradiogram from Case 7, showing enlargement of the heart and especially of the left ventricle (1).

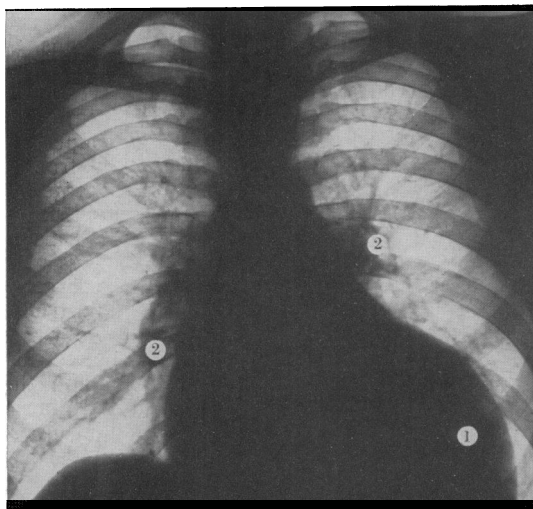


FIG. 19.—Teleradiogram from Case 9, showing great enlargement of the heart and especially of the left ventricle (1) with pulmonary congestion (2).

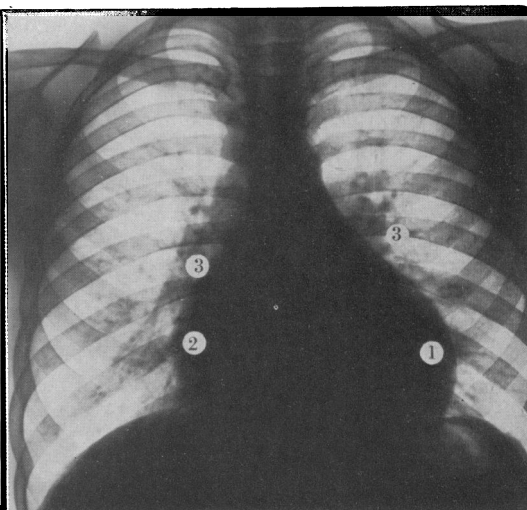


FIG. 20.—Teleradiogram from Case 8 showing generalized enlargement of the heart and especially of the left ventricle (1) and right auricle (2), as well as pulmonary congestion (3).

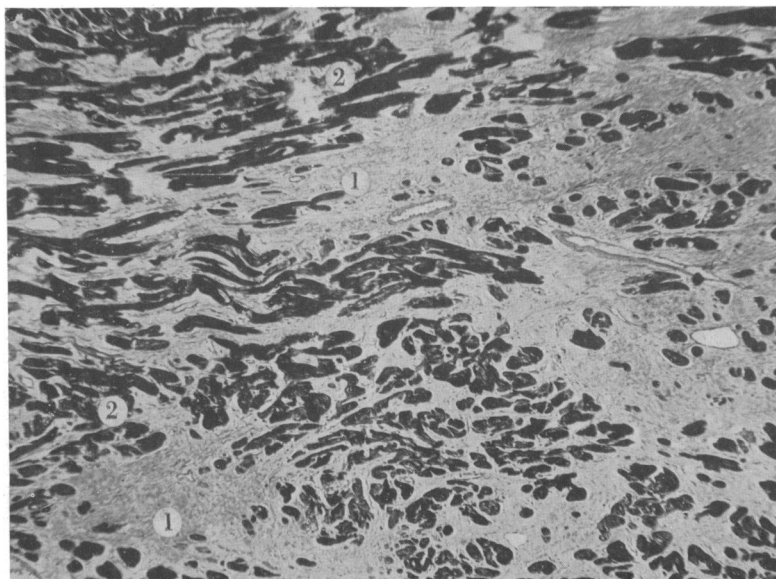


FIG. 21.—Microscopical section of the myocardium from Case 8 showing great fibrosis (1) and hypertrophy of surviving muscle fibres (2).

Case 7. Man, aged 41 years. Although he had complained of breathlessness on exertion for some years he had not sought medical advice, and enlargement of the heart was discovered on routine mass radiography. He had neither palpitation nor giddiness. No other members of the family complained of heart trouble, but none of them was examined.

The pulse was regular and 76 a minute. The blood pressure was 120/85. The apex beat was in the left anterior axillary line. A systolic murmur was heard in late systole in the mitral area and there was prominent splitting of the second heart sound which was confirmed in the phonocardiogram. There were no diastolic murmurs.

There was no enlargement of the liver and no other abnormal physical signs. The urine was clear. The electrocardiogram showed bundle branch block. On cardioscopy (Fig. 18) there was considerable enlargement of the heart especially involving the left ventricle; there was no pulmonary congestion.

Case 8. Boy, aged 12 years. His mother said that for several months he had been subject to attacks of fainting. Three such attacks occurred in the previous fortnight. They had all taken place while he was at school. There was never any warning and he would fall down suddenly. In one attack he hurt his head badly when it banged against the floor. There were no other complaints, and the mother had been told he had epilepsy. There was no family history of a similar illness.

The boy looked healthy. The pulse was rather slow (60 a minute) and was regular. The blood

pressure was low (105/50). The apex beat was out a little way and he showed a short soft systolic murmur. There was triple heart rhythm. No other physical signs presented and there was no enlargement of the liver or spleen. The urine was clear. The cardiogram (Fig. 22) showed sinus rhythm at a slow rate (48 a minute) and a very high voltage. The P-R period was not prolonged nor was the QRS period. There was deviation of the R-T segments, and the T waves were diphasic in certain leads. On cardioscopy (Fig. 20) there was generalized enlargement of the heart and especially of the left ventricle.

He continued to suffer from epileptiform attacks. Four years later, at the age of 16, he developed acute appendicitis and recovered uneventfully from the operation. The day following his discharge from hospital while walking home from the cinema he was seized with severe breathlessness and died on his way to hospital.

At necropsy there was considerable enlargement of the heart (weight not recorded), and particularly of the base of the left ventricle. There was no embolism and no abnormality of the coronary circulation. On microscopical examination there was great hypertrophy of the myocardial fibres of the left ventricle with much interstitial fibrosis (Fig. 21). (See appendix for mother's history.)

Case 9. Man, aged 33 years. He was without symptoms apart from palpitation until three months before when he began to get breathless on exertion. His voice had altered and this brought him to hospital where palsy of the left recurrent laryngeal nerve was found. The pulse was irregular from

extrasystoles and the nature of the arrhythmia was confirmed by the cardiogram (Fig. 23) which also showed wide QRS complexes like those of bundle branch block. The apex beat was displaced outwards as far as the left anterior axillary line and radiological examination confirmed the presence of great enlargement of the heart (Fig. 19). The blood pressure was 120/75. The first heart sound showed splitting and there was a slight systolic murmur in the mitral area. The house physician did not note that any triple heart rhythm was present. There were no other abnormal signs. The urine was clear. The sugar tolerance test was normal and the Wassermann reaction was negative. He left hospital without a definite diagnosis having been made. He died a few months later but there was no necropsy.

DISCUSSION

Unexplained cardiac enlargement is not common. Now and again, however, there comes for diagnosis a patient in whom the cause of an enlarged heart is not obvious. In older patients hypertension may explain cardiac hypertrophy, even though the blood pressure at the time is normal, perhaps reduced by cardiac infarction which can by itself cause a moderate or greater degree of cardiac enlargement. In a younger patient such diagnosis will seldom apply. Bradycardia, with or without heart block, will explain some instances of enlargement of the cardiac silhouette found on radiological examination. An unusual condition like amyloidosis of the heart has been the cause of moderate enlargement in rare cases. Enlargement of the heart from glycogenic disease is even a rarer event in adults. Whenever a single example of unexplained enlargement of the heart is seen the need to find the precise cause has not appeared so important, but when two

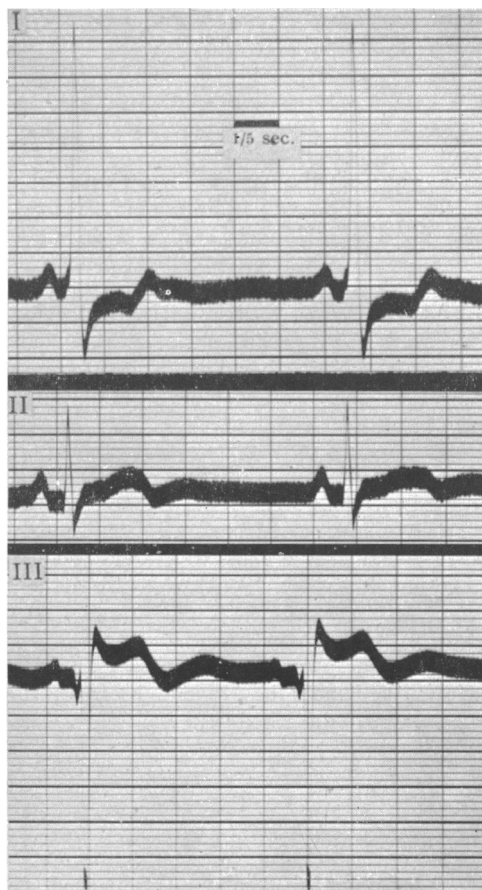


FIG. 22.—Electrocardiogram from Case 8 showing sinus bradycardia, deviation of the R-T segments and diphasic T waves.

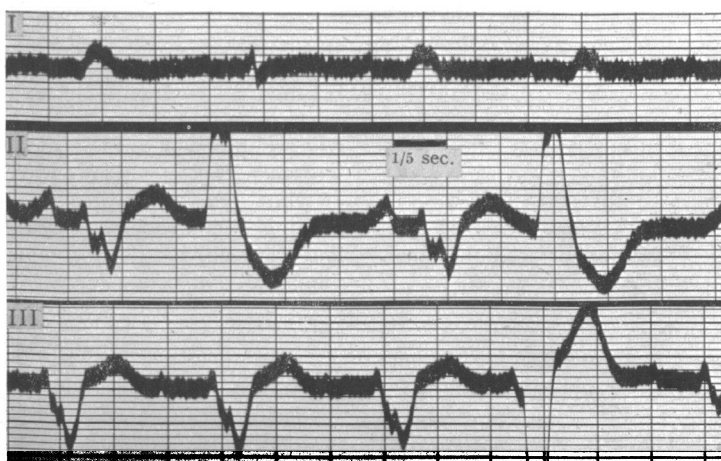


FIG. 23.—Electrocardiogram from Case 9 showing left bundle branch block and extrasystoles.

or more such cases appear, a search for a common aetiology becomes more vital.

When the pathological findings have not been available or are equivocal in these odd instances of cardiac enlargement they have been described under such titles as 'idiopathic enlargement,' or 'unexplained enlargement of the heart in young subjects' (Whittle, 1929; Kugal and Stoloff, 1933; Levy and Rousselot, 1933; Mahon, 1939; Levy and von Glahn, 1937; Case Records of Massachusetts General Hospital, 1942; Norris and Pote, 1946; and Vulliamy, 1947). When inflammatory changes or fibrosis of the myocardium has been an obvious finding at necropsy, they have appeared as acute non-specific myocarditis (Helwig and Wilhelmy, 1939; Candel and Wheelock, 1945), myocardial fibrosis in young men (Sellars and Phillips, 1946), and chronic fibroblastic myocarditis (Ware and Chapman, 1947). Again, the pronounced degree of cardiac enlargement has sometimes been emphasized in a title such as massive cardiac hypertrophy (Doane and Skversky, 1944), while the arrhythmia which is common in such conditions has twice furnished the heading (Major and Wahl, 1932; Addarii, Mahaim, and Winston, 1946). Few of the cases published under these several titles are instances of the condition described here.

In the published cases of obscure cardiac enlargement the metabolism of glycogen has often been discussed. In Case 1 of the present series, deposits of glycogen appeared in many scattered muscle fibres in the left ventricle and the right auricle, and in the vastus externus muscle. Russell (1948) sought to control this finding from the examination of 11 cases at necropsy which took place from 4 to 34 hours after death; they showed scanty amounts of glycogen in the ordinary muscle fibres compared with that found in Case 1 which was examined 56 hours after death. Berlinger (1912) found little glycogen in 25 hearts beyond occasional traces in those cases where necropsy was delayed till five hours after death; the auricular appendage contained more glycogen than other parts. The work of Vallance-Owen (1948), however, has shown that post-mortem material does not appreciably lose its glycogen content up to 50 hours before fixation if kept in a cold chamber; this has corrected the customary belief that when glycogen is found in old post-mortem tissue, more would have been found had fixation of the tissue been carried out immediately after death. The small amount of glycogen found in the liver in Case 1 is without significance for Popper and Wozasak (1930) found glycogen in cases of heart failure. No glycogen was found in the kidney, spleen, or central nervous system in

Case 1. The patients described in this paper are not examples of glycogenic or von Gierke's disease (1929), a condition found in infants where glycogen accumulating in the liver, and rarely in the kidneys and the heart, causes the viscus to enlarge, and where biochemical tests establish a failure in glycogenolysis so that there is ketosis, hypoglycaemia, with absence of the normal rise in the blood sugar after adrenaline, and an abnormal blood sugar curve after glucose, together with a raised blood glycogen and blood cholesterol (Ellis and Payne, 1936). Gardner and Simpson (1938) found 40 reported cases of glycogenic disease, but in none of them had death taken place suddenly or required a medico-legal examination. They recorded the first example of this, a boy aged 11 years. The age of this patient was also exceptional because in the ten previously recorded cases of glycogenic disease in which the presence of excessive glycogen had been demonstrated in the heart muscle, either by Best's stain or by chemical analysis, the ages ranged from 5 weeks to 8 months. Mason and Anderson (1941) have recommended that the term von Gierke's disease should be confined to cases in which there is failure of glycogenolysis. I agree with this view and would add a second criterion, namely, that the designation should be applied to the heart only when it has enlarged from accumulation of glycogen within it. If these rules are applied it is likely that the diagnosis needs to be considered in infants and only rarely in older children or adults.

Of greater significance is the similarity of the signs met with in the present series to those found in Friedreich disease. The familial and hereditary nature of the illness in 3 out of 9 cases is comparable with a series of patients with Friedreich disease where 18 of 38 were the only members of their family to be affected. The heart is commonly affected in Friedreich disease for 12 out of 38 patients showed prominent electrocardiographic changes (Evans and Wright, 1942); such irregularities in the cardiogram told of an interruption of the conducting tissue with complete and bundle branch block, or of involvement of the myocardium producing inversion of the T waves reminiscent of cardiac infarction. Because of the lesser degree of myocardial fibrosis in Friedreich disease, the remarkable widening of the QRS complexes in some of the cases described in this paper, is not found. The size of the heart is not as great in Friedreich disease, but to this finding there are exceptions especially when heart block is present. On pathological grounds too the similarity of Friedreich disease to the condition dealt with here is arresting. Russell (1946), reporting specially on the heart in four cases of Friedreich

disease, found a piece-meal destruction of muscle fibres with fibrosis and hypertrophy of the surviving fibres, and remarkably little cellular inflammatory infiltration; there was no glycogen in one heart, but it was not sought specially in the other three. Naturally, the relation of this condition to Friedreich disease would be more definitely established if instances of each were met with in one family, but such a coincidence has not so far come to my notice.

SUMMARY

There is described in this paper a distinct syndrome having a definite clinical, cardiographic, and pathological pattern.

Clinically it is characterized by light symptoms at the start, and is often found fortuitously in a young adult during routine examination preliminary to admission to military service or civilian occupation. Ultimately, palpitation, momentary giddiness, and frank Stokes-Adams attacks may develop, and death may come suddenly during such episodes, or as the result of heart failure precipitated by the onset of paroxysmal tachycardia.

On examination the pulse is usually irregular from extrasystoles, paroxysmal tachycardia, auricular fibrillation, or heart block. There is great enlargement of the heart, and the blood pressure is normal. The heart sounds are usually clear, and there is either splitting of the second sound, or triple heart rhythm from the addition of the third heart sound. There is no enlargement of the viscera, and serological tests and the blood chemistry are normal.

The *electrocardiogram* shows extrasystoles, paroxysmal tachycardia, auricular fibrillation, or heart block, according to the kind of arrhythmia prevailing at the time; the QRS complexes are usually exceptionally wide, depending on the extent of the fibrosis and the size of the heart, and the T waves are inverted.

On *cardioscopy* there is enlargement of the heart, and as a rule the cardiomegaly is considerable.

The *prognosis* depends on the extent of the fibrosis and the associated cardiac enlargement. Thus, it is poor in young subjects with great enlargement of the heart, but in older subjects with moderate cardiac enlargement the outlook can be favourable although recurrent Stokes-Adams attacks are a handicap if frequent.

Pathologically the condition shows fibrosis of the myocardium is usually conspicuous; this is associated with hypertrophy of the remaining muscle fibres producing great cardiac enlargement. Intracardiac thrombosis initiating embolism is an

expected complication. Although glycogen may be present and even in slight excess of the normal, the syndrome described here should be regarded as a separate entity from glycogenic or von Gierke's disease—is usually confined to young children or infants—where a viscus becomes distended by the large accumulation of glycogen within it, and where laboratory tests during life show faulty glycogenolysis. Neither does the syndrome include those cases of hypertrophy of muscle fibres in the absence of myocardial fibrosis.

The *etiology* of the condition, although obscure, probably rests with an unknown factor which in Friedreich disease involves the central nervous system alone or along with the heart, and in the condition described here affects the heart exclusively, causing myocardial fibrosis. Like Friedreich disease too the condition may be familial and hereditary, or it may arise sporadically and *de novo*.

Having regard to the specificity of the condition and its chief characteristics I propose to name it *Familial Cardiomegaly*.

APPENDIX

Since this paper was written the mother of Case 8 has been admitted to hospital. She is 42 years of age and for two months has experienced short attacks of paroxysmal tachycardia. Once she lost consciousness for six minutes. Her pulse is regular and the blood pressure normal. The apex beat is in the left anterior axillary line. There are no murmurs. A triple heart rhythm from addition of the fourth heart sound is caused by delayed A-V conduction and there is splitting of the second sound in the mitral area from bundle branch block; these findings have been confirmed by the phonocardiograph. The electrocardiogram shows a prolonged P-R period and bundle branch block. On cardioscopy there is considerable generalized enlargement of the heart and much pulmonary congestion. She is, therefore, another example of familial cardiomegaly, her son, Case 8, having died suddenly at the age of 16 from the same condition. The addition of this patient to Cases 1, 2, 3, and 8 supplies five instances of the disease where a family history of the complaint was present.

I wish to thank Professor Dorothy Russell, not only for reporting on the pathological findings in Case 1, but also for her helpful discussion of the significance of these findings.

Sir John Parkinson, Physician to the Cardiac Department, has given me advice on the writing of this paper. Dr. Maxwell Chance referred Case 1 to me and in this way enabled me to examine a brother (Case 2) and his mother (Case 3). Dr. Francis Camps supplied me with the details of necropsy in Case 8.

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